identifying the patient as having a *Helicobacter pylori* infection if the *Helicobacter pylori* nucleic acid is detected.

AS cond

23. (New) The method of claim 22, wherein the *Helicobacter pylori* nucleic acid is at least 175 nucleotides long.

RESPONSE

Claims 1-18 were pending in this application. Claims 10-16 are cancelled without prejudice, claims 1-3, 5, 8, 9, and 18 are amended, and new claims 19-23 are added by the present amendment. A marked-up copy of the amended claims in accordance with 37 C.F.R. § 1.121(c)(1)(ii) is enclosed. Claims 1-9 and 17-23 are pending and presented for consideration.

Claim 1 is amended to recite detecting a *Helicobacter pylori* nucleic acid present in a patient stool sample and having a length exceeding a reference length, and identifying the patient as having a current *Helicobacter pylori* infection if the nucleic acid is present in an amount exceeding a reference amount. Support for the amendment is found throughout the originally-filed application and at least, for example, at page 3 and in originally-filed claim 6.

Claim 2 is rewritten in independent form and is amended to recite detecting a high-integrity *Helicobacter pylori* nucleic acid, comparing an amount of high-integrity *Helicobacter pylori* nucleic acid to an amount of a non-*Helicobacter pylori* nucleic acid, and identifying a patient as having a current *Helicobacter pylori* infection if the relative amount of high-integrity *Helicobacter pylori* nucleic acid and of non-*Helicobacter pylori* nucleic acid exceeds a reference relative amount. Support for the amendment is found throughout the originally-filed application and at least, for example, at pages 2 and 5 and in originally-filed claim 1.

Claim 3 is amended to recite a human nucleic acid. Support for the amendment is found throughout the originally-filed application and at least, for example, at pages 8, 11, 16, and 17.

Claim 5 is amended to depend from claim 2.

Claim 8 is amended to depend directly from claim 1.

Claim 9 is amended to delete a recitation of preserving integrity of a *Helicobacter pylori* nucleic acid.

Claim 18 is amended to recite detecting a human nucleic acid and identifying a patient as having disease if the length of the nucleic acid exceeds a reference length. Support for the amendment is found throughout the originally-filed application and at least, for example, at pages 3, 8, 11, 16, and 17.

Support for new claim 19 is found throughout the originally-filed application and at least, for example, at page 2. Support for new claim 20 is found throughout the originally-filed application and at least, for example, at page 3. Support for new claim 21 is found throughout the originally-filed application and at least, for example, at page 4, and in originally-filed claim 17. Support for new claim 22 is found throughout the originally-filed application and at least, for example, at pages 9, 10, and 13, in Figures 1 and 2, and in originally-filed claim 1. Support for new claim 23 is found throughout the originally-filed application at least, for example, at page 2.

Applicant submits that no new matter has been added.

Information Disclosure Statement

Applicant thanks Examiner Chunduru for indicating that the Information Disclosure Statement has been entered. Applicant has not yet received a copy of the initialed 1449 forms, and requests that a copy be mailed to the correspondence address of record or faxed (617-248-7970) to the attention of the undersigned agent to complete Applicant's files.

Claim Objection

The Office Action objected to claim 18 as being a substantial duplicate of claim 1. Applicant has amended claim 18 to clarify the differences between claim 18 and claim 1. For example, claim 18 recites detecting a human nucleic acid, whereas claim 1 recites detecting a *Helicobacter pylori* nucleic acid. Applicant submits that the claims therefore cover distinct subject matter, and requests reconsideration and withdrawal of the objection.

Claim Rejections Under 35 U.S.C. § 112

The Office Action rejected claims 1-9 and 18 under 35 U.S.C. § 112, second paragraph, alleging that "determining integrity" and "predetermined threshold" are unclear and indefinite. As amended, none of the pending claims recites "determining integrity" or "predetermined threshold." As suggested by the Office Action, claims 1, 2, and 18 now refer to reference lengths (claims 1 and 18), amounts (claim 1), and relative amounts (claim 2). Accordingly, Applicant submits that the claims comply with 35 U.S.C. § 112.

Applicant requests reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 102(b)

Chong et al., *J. Clin. Microbiol. 34(11):2728-2730 (1996) ("Chong")*

The Office Action rejected claims 1-6, 8, and 17-18 under 35 U.S.C. § 102(b) as anticipated by Chong. Applicant traverses this rejection.

Independent claims 1, 2, 17 and 18 (and dependent claims 3-6 and 8) relate to methods for detecting a *Helicobacter pylori* infection. Chong does not disclose or suggest a method for detecting a *Helicobacter pylori* infection. Chong discloses that PCR using primer set Hp1-Hp2 amplifies a 109-bp product in "human tissue samples taken from *H. pylori*-infected *and uninfected* patients" and in human leukocyte samples and a human cell line (Abstract, emphasis added). Chong deduces that "the Hp1-Hp2 PCR produces false positive results" because "the 109-bp fragment was amplified by the Hp1-Hp2 PCR of DNA from the human genome" (p.2729). Chong concludes that PCR using that primer set "is not specific and cannot be used to detect *H. pylori* in clinical specimens" (Abstract). Accordingly, Chong does not disclose or suggest a method for detecting a *Helicobacter pylori* infection, and does not disclose or suggest identifying a patient as having a "*Helicobacter pylori* infection" (per independent claims 1, 2, or 17) or "disease" (per independent claim 18) based on such a method. Applicant therefore requests reconsideration and withdrawal of this rejection.

Li et al., J. Clin. Pathol. *48:662-666 (1992) ("Li")*

The Office Action rejected claims 1-3, 5, 7-8 and 18 under 35 U.S.C. § 102(b) as anticipated by Li. Applicant traverses this rejection.

Amended independent claim 1 recites detecting a *Helicobacter pylori* nucleic acid present in a patient stool sample. Li does not teach detecting *Helicobacter pylori* nucleic acid present in a patient stool sample. Applicant therefore submits that neither independent claim 1 nor any claim depending therefrom is anticipated by Li. Applicant further submits that independent claim 1 is not obvious in view of Li. Applicant notes that, according to Chong, "the lack of a positive Hp1-Hp2 PCR result [in stool samples] is very likely due to the presence of PCR inhibitors in stool specimens" (Chong, p. 2730). Applicant therefore submits that one skilled in the art would not be motivated to try to substitute stool samples for the gastric biopsy and saliva samples of Li, and would not have had a reasonable expectation of success in doing so.

Amended independent claim 2 recites comparing an amount of high-integrity *Helicobacter pylori* nucleic acid present in a patient sample to an amount of a non-*Helicobacter pylori* nucleic acid present in the patient sample. Li does not teach or suggest comparing to an amount of a non-*Helicobacter pylori* nucleic acid present in the patient sample. Li's "negative sample to compare with the positive samples" (Office Action, p. 4) is not a sample from the patient; rather, Li's "negative samples" are, for example, biopsy specimens from known *H. pylori*-negative patients (Figure 2), or genomic DNAs from other bacteria (Li, p. 664, second column). Because Li does not teach or suggest comparing to an amount of a non-*Helicobacter pylori* nucleic acid present in the patient sample, Li cannot anticipate or render obvious the invention of amended independent claim 2.

Amended independent claim 18 recites detecting a human nucleic acid and identifying the patient as having disease if the length of the nucleic acid exceeds a predetermined threshold. Li does not teach or suggest detecting a human nucleic acid, or identifying a patient having disease if the length of the nucleic acid exceeds a predetermined threshold. Accordingly, Applicant submits that Li does not anticipate or render obvious independent claim 18.

Applicant requests reconsideration and withdrawal of this rejection.

Claim Rejection Under 35 U.S.C. § 103

The Office Action rejected claim 9 under 35 U.S.C. § 103 as unpatentable over Chong in view of U.S. Patent No. 6,143,529 ("Lapidus"). Applicant traverses this rejection.

Chong does not disclose or suggest a method for detecting a *Helicobacter pylori* infection. According to Chong, the Hp1-Hp2 PCR primer set generates false positives from uninfected patients "and cannot be used to detect *H. pylori* in clinical specimens" (Abstract). Applicant submits that a skilled artisan would not be motivated to modify Chong by adding an ion chelator. There is no teaching or suggestion that adding an ion chelator would abrogate the false positive problems identified by Chong and permit detection of a *Helicobacter pylori* infection. Applicant submits that a skilled artisan would not have had a reasonable likelihood of success in eliminating the false positives through addition of an ion chelator. Furthermore, like Chong, Lapidus does not teach or suggest a method for detecting *H. pylori* and does not teach or suggest identifying a patient as having a current *Helicobacter pylori* infection if a *Helicobacter pylori* nucleic acid is present in a patient sample in an amount exceeding a predetermined threshold as recited in independent claim 1 from which claim 9 depends. Accordingly, Applicant submits that claim 9 cannot be rendered obvious by the cited references.

Applicant requests reconsideration and withdrawal of this rejection.

CONCLUSION

Claims 1-9 and 17-23 are pending and presented for consideration. Examiner Chunduru is invited to telephone the undersigned agent to discuss any remaining issues. Applicant believes that no fee and no extension of time are required for entry and consideration of this paper. Nevertheless, if either is required, please consider this a conditional petition for any required extension and authorization to charge any required fee to Deposit Account No. 20-0531.

Respectfully submitted,

Date: May 13, 2002
Reg. No. 48,645

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MARKED-UP COPY OF CLAIMS AS AMENDED
U.S.S.N. 09/755,004

(Amended) A method for detecting a *Helicobacter pylori* infection, the method comprising the steps of:

[determining an integrity of] detecting a *Helicobacter pylori* nucleic acid present in a patient stool sample and having a length exceeding a reference length; and

identifying the patient as having a current *Helicobacter pylori* infection if the [integrity of the] nucleic acid [exceeds a predetermined threshold] is present in an amount exceeding a reference amount.

2. (Amended) [The method of claim 1, wherein the identifying step comprises] A method for detecting a *Helicobacter pylori* infection, the method comprising the steps of:

[comparing the integrity of the] detecting a high-integrity *Helicobacter pylori* nucleic acid present in a patient sample;

[to an integrity] comparing an amount of high-integrity *Helicobacter pylori* nucleic acid present in the patient sample to an amount of a non-*Helicobacter pylori* nucleic acid present in the patient sample; and

identifying the patient as having a current *Helicobacter pylori* infection if the relative amount of high-integrity *Helicobacter pylori* nucleic acid and of non-*Helicobacter pylori* nucleic acid exceeds a reference relative amount.

3. (Amended) The method of claim 2, wherein the non-*Helicobacter pylori* nucleic acid is a [patient] human nucleic acid.

5. (Amended) The method of claim [1]2, wherein the patient sample is selected from the group consisting of stool, sputum, pancreatic fluid, bile, lymph, blood, urine, saliva, gastric juice, and vomitus.

8. (Amended) The method of claim [5]1, wherein the *Helicobacter pylori* nucleic acid is a DNA.

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9. (Amended) The method of claim 1, comprising the further step of adding an ion chelator to the patient sample such that the concentration of the ion chelator is at least 150 mM [, thereby to preserve the integrity of the *Helicobacter pylori* nucleic acid].

18. (Amended) A method for detecting a *Helicobacter pylori* infection in a patient, the method comprising the steps of:

detecting a [patient] <u>human</u> nucleic acid in a patient sample comprising shed cells or cellular debris; and

identifying the patient as having disease if the length of the nucleic acid exceeds a [predetermined threshold] <u>reference length</u>.